



NOTES

ENDOCRINE TUMORS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Tumors arising from endocrine gland tissue
- May be functional (excess secretion of one/more hormones); nonfunctional (clinically silent)

SIGNS & SYMPTOMS

- Depends on degree of hypersecretion, mass effect

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Tumor visualization, staging

LAB RESULTS

- Measure hypersecretion degree

OTHER DIAGNOSTICS

- History, physical examination with characteristic findings

TREATMENT

MEDICATIONS

- Chemotherapy
- Hormone replacement/suppression

SURGERY

- Resection

OTHER INTERVENTIONS

- Radiation therapy
- Address complications

ADRENAL CORTICAL CARCINOMA

osms.it/adrenal-cortical-carcinoma

PATHOLOGY & CAUSES

- Rare, malignant adrenal cortex tumor
- Usually functional, with excess hormone secretion
 - Glucocorticoids → Cushing's syndrome
 - Androgens → virilization (biologically-female individuals), feminization (biologically-male individuals)
 - Aldosterone (rare) → hyperkalemia

RISK FACTORS

- Biologically female
- **Bimodal distribution:** ages 0–5, 40–50
 - **Adults:** more aggressive
- Associated with hereditary cancer syndromes (e.g. MEN1, Li-Fraumeni syndrome)

COMPLICATIONS

- Metastasis (renal vein, para-aortic nodes, lungs), diabetes

VISIT...

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SIGNS & SYMPTOMS

- Rapidly progressing hypercortisolism signs
 - ↑ weight, muscle wasting, fat redistribution, skin atrophy
- Hyperandrogenism
 - **Female:** hirsutism, male-pattern baldness, oligomenorrhea
 - **Male:** gynecomastia, testicular atrophy, erectile dysfunction
- Mass effect
 - Abdominal, flank pain; nausea; vomiting

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Usually unilateral, irregular shape, heterogeneous; presence of necrosis, calcification; tumor staging (local invasion/distant metastases)

LAB RESULTS

- Measure hypersecretion degree
 - Fasting blood glucose, potassium, basal cortisol, corticotropin (ACTH), 24-hour urinary free cortisol, sex hormones (e.g. dehydroepiandrosterone, androstenedione, testosterone, 17-hydroxyprogesterone, 17-beta-estradiol)

TREATMENT

MEDICATIONS

- Chemotherapy

SURGERY

- Resection

OTHER INTERVENTIONS

- Radiation therapy

PITUITARY ADENOMA

osms.it/pituitary-adenoma

PATHOLOGY & CAUSES

- Benign anterior pituitary tumor arising from specific cell types
 - Eventual normal pituitary tissue destruction → [hypopituitarism](#)
- Associated with genetic mutations
 - Loss-of-function mutations ([MEN1](#))
 - Activating mutation in guanine nucleotide stimulatory protein ([Gs-alpha](#))
 - Overexpression of pituitary tumor transforming gene ([PTTG](#))
 - Expression of truncated form of fibroblast growth factor receptor ([FGF-4](#))
- Monoclonal tumor formation → adjacent structure compression (e.g. meninges,

optic nerve/chiasm) + specific hormone hypersecretion

Classification

- **Microadenoma:** < 1cm/0.4in
- **Macroadenoma:** > 1cm/0.4in
- **Functional, non-functional**

TYPES

- Gonadotroph adenomas usually non-secreting/may cause hypogonadism
- **Prolactinomas** → [hyperprolactinemia](#), galactorrhea, hypogonadism
 - [Lactotroph/somatotroph](#) adenoma (rare plurihormonal adenomas) secrete prolactin, growth hormone (GH)
- **Somatotroph adenomas** secrete GH → [acromegaly](#) (adults); [gigantism](#) (children)
- **Corticotropin** (adrenocorticotrophic hormone)

[ACTH)]-secreting adenomas → Cushing's syndrome

- Thyrotropin-secreting tumors → hyperthyroidism

RISK FACTORS

- Genetic predisposition, sporadic development

COMPLICATIONS

- Mass effect, pituitary apoplexy (hemorrhage into pituitary), sella turcica erosion, hormone-related disease development (e.g. Cushing syndrome), panhypopituitarism

SIGNS & SYMPTOMS

- Adjacent structure compression
 - Visual changes (e.g. diplopia, bitemporal hemianopsia), headache

DIAGNOSIS

DIAGNOSTIC IMAGING

Gadolinium-enhanced MRI

- Delineates tumor boundary; proximity to optic chiasm, cavernous sinus; tumor consistency; hemorrhage/cystic lesion presence
 - T1-weighted: hypointense
 - T2-weighted: hyperintense

LAB RESULTS

- Pituitary hormone hyper-/hyposecretion

TREATMENT

MEDICATIONS

- Replacement hormones (e.g. hydrocortisone, synthroid for hypopituitarism)
- Hormone suppression (e.g. somatostatin analogs for GH-secreting hormones; dopamine agonists for lactotrophs)

SURGERY

- Transsphenoidal tumor resection
- Stereotactic radiosurgery (gamma knife)

OTHER INTERVENTIONS

- Radiation therapy

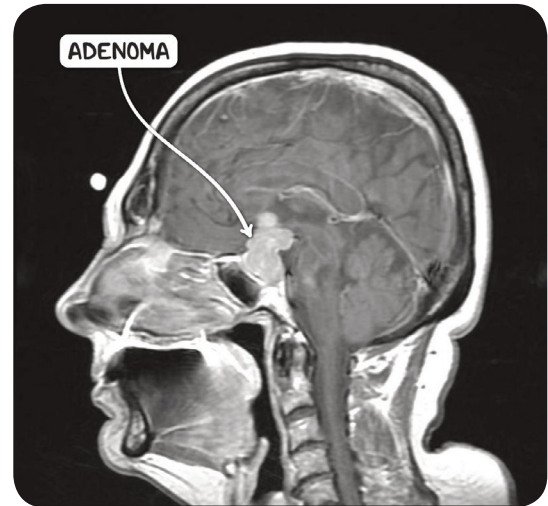


Figure 15.1 An MRI scan of the head in the sagittal plane demonstrating a large pituitary adenoma.

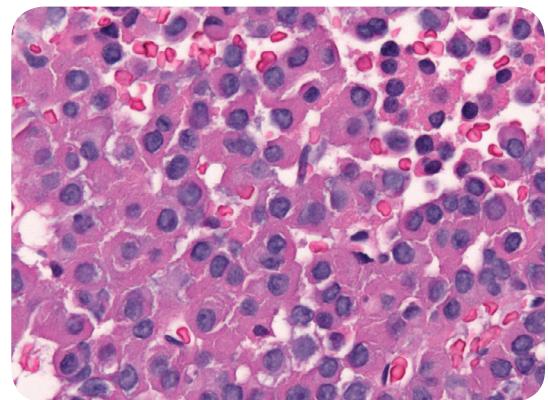


Figure 15.2 The histological appearance of a pituitary adenoma. The finely granular eosinophilic cytoplasm seen here is characteristic of a growth hormone producing adenoma. The lobular architecture of normal pituitary tissue is lost.

PROLACTINOMA

osms.it/prolactinoma

PATHOLOGY & CAUSES

- Functional, usually benign **lactotroph cell tumor** in anterior **pituitary** → prolactin (PL) secretion, prolactinemia
 - **Rarely:** tumors arise from both lactotroph, somatotroph cells → secrete growth hormone (GH), and PL
 - Malignant pituitary PRL-secreting carcinomas (rare)
- Monoclonal tumor formation → adjacent structure compression (e.g. meninges, optic nerve/chiasm) + **prolactin hypersecretion** → milk production stimulation; secondary gonadal function effects

Classification

- **Microadenoma:** < 1cm/0.4in
- **Macroadenoma:** > 1cm/0.4in

RISK FACTORS

- Biologically female
- Peak incidence during childbearing years
- May be associated with MEN1

COMPLICATIONS

- Hypothalamic-pituitary stalk compression → hypopituitarism
- Gonadal steroidogenesis impairment → **infertility**
- **Hypogonadism**-induced ↓ bone-mineral density → **osteoporosis** (biologically-female individuals)
- Male/female infertility

SIGNS & SYMPTOMS

- Microprolactinomas may be asymptomatic
- **Biologically-female individuals:** **galactorrhea**, **amenorrhea**, vaginal dryness
- **Biologically-male individuals:** gynecomastia, erectile dysfunction
- Mass effects → visual problems, headaches

DIAGNOSIS

DIAGNOSTIC IMAGING

Gadolinium-enhanced MRI

- Delineates tumor boundary; proximity to optic chiasm, cavernous sinus; tumor consistency; hemorrhage/cystic lesion presence

LAB RESULTS

- ↑ serum prolactin

TREATMENT

MEDICATIONS

- Dopamine agonists

SURGERY

- Transsphenoidal resection
- Stereotactic radiosurgery (gamma knife)

OTHER INTERVENTIONS

- Radiation therapy

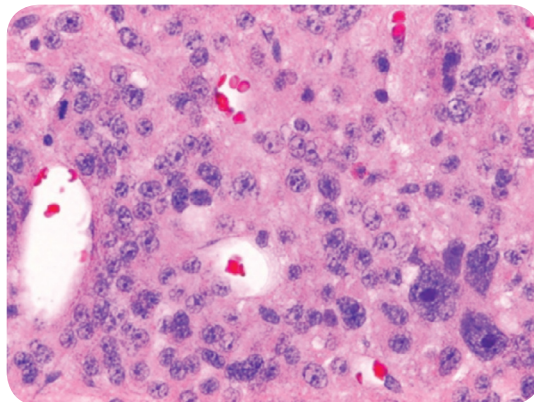


Figure 15.3 The histological appearance of a prolactinoma. The cells have moderate amounts of eosinophilic cytoplasm and finely granular nuclear chromatin.

THYROID CANCER

osms.it/thyroid-cancer

PATHOLOGY & CAUSES

- Uncommon thyroid gland carcinoma
- **Predominance:** biologically-female adults
- Derived from thyroid's follicular epithelium
 - Except medullary thyroid carcinoma → functional parafollicular C cells

TYPES

Papillary thyroid

- **Most common**, least aggressive
- Multiple projections arise from follicular cells growing towards blood vessels, lymphatics; papillae = small projection/outgrowth
 - Lymphatic spread to cervical lymph nodes
- May be part of inherited syndrome (Cowden syndrome, Gardner syndrome)
- Light microscopy
 - Cells with empty nuclei, AKA "Orphan Annie eyes"

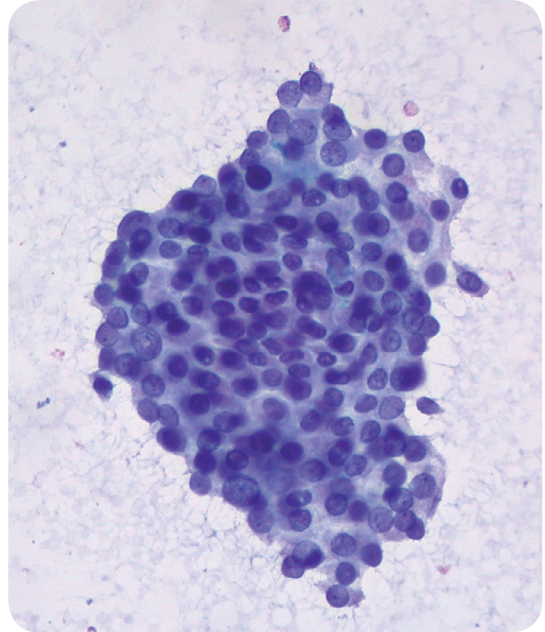


Figure 15.4 The cytological appearance of papillary thyroid carcinoma following fine needle aspiration. There are large cell clusters in a papillaroid configuration. The cell nuclei are of variable size.



Figure 15.5 The gross pathological appearance of an anaplastic thyroid carcinoma which has replaced an entire thyroid lobe.

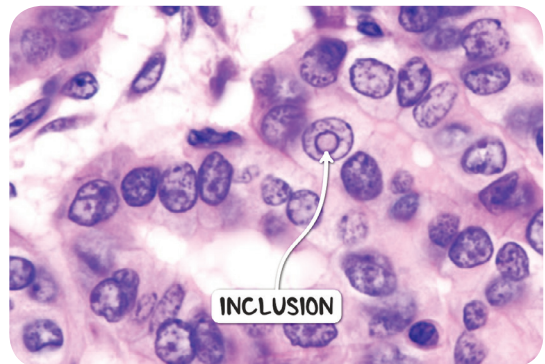


Figure 15.6 The histological appearance of thyroid papillary carcinoma at high magnification demonstrating nuclear inclusion bodies and pale chromatin with a dark nuclear envelope giving the classic orphan Annie appearance.

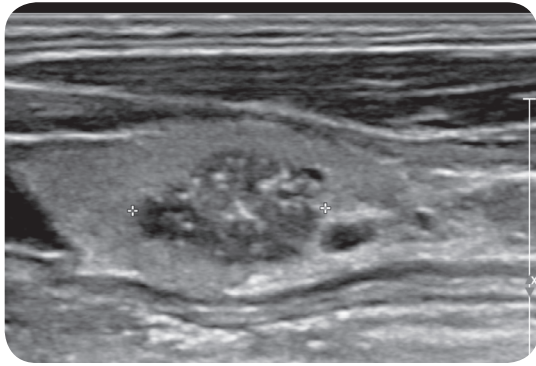


Figure 15.7 An ultrasound image of the left lobe of the thyroid demonstrating a papillary carcinoma. The tumor is well circumscribed and hypoechoic with visible microcalcifications.

Follicular thyroid

- AKA follicular adenocarcinoma; second most common
- Follicular cell invasion of thyroid capsule → blood vessel invasion → hematogenous spread to bone, liver, brain, lungs
 - Distant metastasis in some cases
- Well-circumscribed single nodules with colloid filled follicles; may be calcified, have central fibrosis
- May present with eosinophilic cells with granular cytoplasm; AKA Hürthle cells

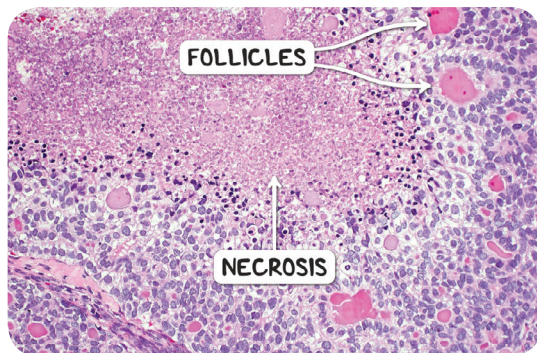


Figure 15.9 The histological appearance of follicular thyroid carcinoma. The tumor cells form vague follicular structures and there is abundant central necrosis.

Medullary thyroid carcinoma

- Arises from functional parafollicular C cells; in upper 1/3 of gland
 - Calcitonin secretion → breakdown → deposits in extracellular thyroid space → amyloid
- 1/3 familial, 1/3 sporadic, 1/3 associated with MEN 2A, 2B
- Germline RET mutations → abnormal receptor activation → cancer
- Light microscopy
 - Spindle shaped cells; myloid deposits

Anaplastic/undifferentiated carcinomas

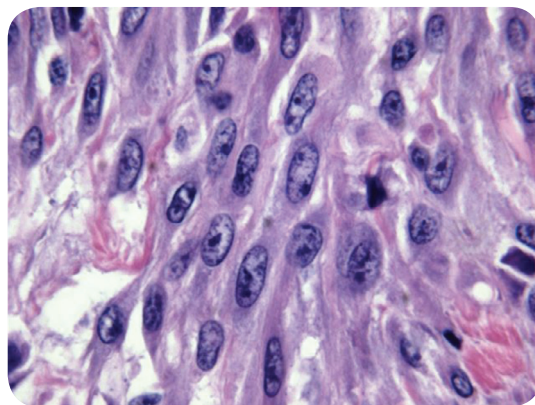


Figure 15.8 The histological appearance of a spindled anaplastic thyroid carcinoma.

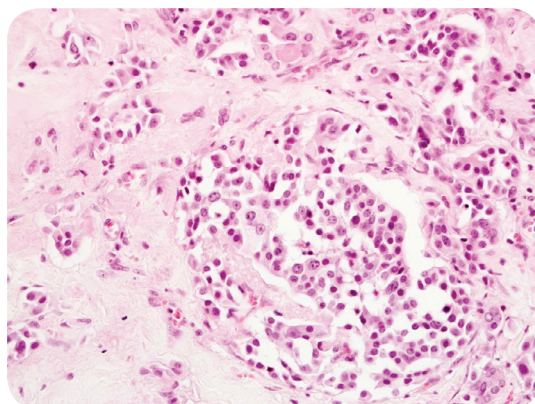


Figure 15.10 The histological appearance of medullary thyroid cancer. The nuclear chromatin displays a classic salt and pepper pattern.

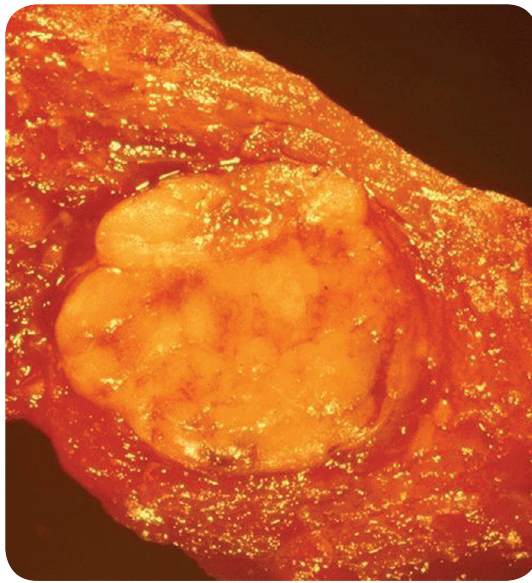


Figure 15.11 The gross pathological appearance of medullary carcinoma of the thyroid gland. The tumor is well circumscribed occupying a single thyroid lobe with a fleshy cut surface.

CAUSES

- Gain-of-function mutations in growth factor signaling pathways
 - Except medullary thyroid carcinoma

RISK FACTORS

Papillary thyroid

- *Childhood ionizing radiation exposure:* ionizing radiation → RET + BRAF proto-oncogene activation → cancer

Follicular thyroid

- *Iodine deficiency:* RAS, PIK3CA proto-oncogene activation + PTEN tumor suppressor gene inactivation → cancer

SIGNS & SYMPTOMS

- Large, solitary, painless, thyroid nodule (hard consistency, fixed)
- May impair thyroid hormone production → hypothyroidism
 - Weight gain, fatigue, cold intolerance
- Mass effect
 - Hoarseness, trouble swallowing

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound

- Thyroid
 - Solid vs. cystic thyroid nodule (most cancers solid)

LAB RESULTS

- Thyroid hormone levels

Fine needle aspiration

- Confirm diagnosis (benign vs. malignant)

Thyroid scan

- When fine needle aspiration indeterminate

TREATMENT

SURGERY

- Resection, adjuvant treatment